Rubella

Before we begin with rubella, I would like to make a few comments about mumps. We do not have time during this program to discuss mumps in detail. The number of reported mumps cases has declined by more than 90% in the last decade. In 1990, about 5,200 cases were reported. In 2002, only 270 cases were reported. There are two reasons for this remarkable decline. First, most states now require evidence of mumps immunity for school entry. Second, and most importantly, is the recommendation that the second dose of measles vaccine be given as MMR. As with measles vaccine, 5% or so of MMR recipients fail to respond to the first dose of mumps vaccine. The second dose of MMR gives recipients a second chance to develop immunity to mumps as well as measles. The net effect of both these factors is that very few children remain susceptible to mumps, and the disease has disappeared. It is likely that indigenous transmission of mumps virus will be interrupted in the U.S., as it has been for measles and rubella.

We get a lot more questions about rubella and rubella vaccine than about mumps, so we will spend a few minutes discussing it. The chapter begins on page 145 if you would like to follow along.

Rubella was first described as a distinct clinical entity in German literature in the 18th century-hence the common name "German measles". Prior to that time, most physicians took it to be a variant of measles or a combination of measles and scarlet fever. The name rubella, or "little red" in Latin, was first used in 1841 by a British physician who described an outbreak in India. No one paid much attention to "little red" for 100 years, until 1941, when Norman Gregg, an Australian ophthalmologist, recognized the connection between maternal rubella infection and congenital cataracts and heart defects. He was knighted by the queen of England for that observation.

Rubella virus was first isolated in 1962. About the same time, a pandemic of rubella occurred in Europe and America. Thousands of families suffered because of the miscarriages and birth defects caused by rubella. This helped stimulate the development of a vaccine.

Rubella is a togavirus with an RNA genome. There is only one antigenic type. The virus is rapidly inactivated by heat and light, so it does not persist long in the environment.

The incubation period of rubella is 12 to 23 days, but averages 14 to 16 days. There may be a prodrome consisting of low grade fever and malaise. Lymphadenopathy, or enlarged lymph nodes, may appear in the second week.

The rash appears 14 to 17 days after exposure. Rubella is generally a mild illness. In fact, up to half of infections are inapparent or subclinical.

Here is a short video that shows a child with a moderate case of rubella.

THIS CHILD HAS RUBELLA. THE RUBELLA RASH USUALLY BEGINS, AND IS MOST NOTICEABLE ON THE FACE, BUT MAY INVOLVE OTHER PARTS OF THE BODY. THE RASH USUALLY LASTS ABOUT 3 DAYS, HENCE ITS COMMON NAME OF 3 DAY MEASLES. THESE ARE THE ENLARGED POSTAURICULAR LYMPH NODES SEEN FREQUENTLY WITH RUBELLA. POSTERIOR CERVICAL AND SUBOCCIPITAL NODES MAY ALSO BE INVOLVED. NOTICE THAT THE RASH IS MUCH MORE SPARSE ON THE TRUNK AND ARMS THAN ON THE FACE. THE RASH IS TYPICALLY FAINTER THAN A MEASLES RASH AND DOES NOT COALESCE. THE RASH IS MORE PROMINENT AFTER A HOT SHOWER OR BATH.

There are a few complications of rubella that you should be aware of, since similar symptoms occur as adverse reactions following vaccination. The most common are arthralgia, or joint pain, and arthritis, or inflammation of a joint. Joint symptoms are rare in children. But joint symptoms are reported in up to 30% of adults, and in 50% to 70% of adult females with rubella. Chronic and recurrent joint symptoms have also been described following rubella in adult women. Thrombocytopenic purpura occurs once in 3,000 cases, and encephalitis is reported once in 5,000 to 6,000 cases.

The real public health significance of rubella is not the disease itself, nor its complications. It is congenital infection. The virus may infect many different embryonic cell lines, and so may damage many different organs. Collectively, these abnormalities are known as congenital rubella syndrome, or CRS. Unfortunately, the mother does not have to be symptomatic to transmit the virus to the fetus. Inapparent infections in the mother may lead to CRS. In general, the younger the fetus when infected, the more serious the damage. Up to 90% of infants born to women infected with rubella virus in the first 11 weeks of pregnancy will have defects. Infection early in pregnancy may also lead to fetal death and miscarriage. Fortunately, CRS is rare with second trimester infection. Here is a list of some of the most common anomalies associated with CRS. The most common defects are the classic triad of deafness, cataracts, and heart defects. Microcephaly, or small head, is common. Mental retardation is also common, and may not become apparent until the child is a few years old. These are just a few of the common abnormalities. Defects have been described in virtually every organ. This child has congenital cataracts, one of the most common findings in congenital rubella syndrome. Infants born with CRS may have other eye defects, such as glaucoma and retinal abnormalities. Many children with congenital rubella syndrome are permanently disabled. The good news is that virtually every case of CRS could be prevented with a single dose of rubella vaccine.

Rubella is a human disease, and the reservoir is acutely infected persons. There is no animal or insect vector of rubella virus. Transmission of rubella is respiratory. It is communicable 7 days before to 5 to 7 days after rash onset. But

subclinical or asymptomatic cases may transmit. Infants infected in utero with rubella virus may shed virus for a year or more.

This graph shows the number of rubella cases reported by year since 1966, when the disease became nationally reportable. That year there were 47,000 cases and 12 deaths. Rubella peaked in 1969 with 58,000 cases and 29 deaths. Following licensure of the first rubella vaccines, cases fell rapidly to 12,000 in 1979.

This graph shows reported rubella cases by year since 1980. Since 1983, fewer than 1,000 cases of rubella have been reported annually, except in 1990, with 1,100 cases, and 1991, with 1,400 cases. These increases were due to large outbreaks, in California in 1990 and among the Amish, mostly in Pennsylvania in 1991. This next graphic overlays the number of reported cases of congenital rubella syndrome, shown in the blue line. Notice the similarity in the shapes of the rubella and CRS lines. CRS fell along with rubella in the early 1980s. This little peak of CRS in 1986 was a cluster of cases in New York City that was not associated with an increase in reported rubella. The big peak follows a rubella outbreak in California in 1991, and following an outbreak among the Amish in Pennsylvania in 1992.

It is possible that indigenous transmission of rubella virus has been interrupted. An all time low of 18 cases of rubella were reported in 2002. A provisional total of 7 cases was reported in 2003. One infant with CRS was reported in 2001 and none were reported in 2002 or 2003.

This graphic shows the age distribution in percent of reported rubella cases from 1982 to 2002. During most of these years, there was no predominant age group. But in the last several years, an increasing number of cases have been reported in persons 15 to 39 years of age, in the blue line. In 2002, this age group accounted for 72% of all cases of reported rubella. This age shift is particularly unfortunate because the 15 to 39 years age group includes childbearing age – the worst possible time to get rubella. If we wish to reduce the burden of congenital rubella syndrome, it is critical to prevent rubella among women of reproductive age.

Until recently most countries of the world, including most in Latin America, did not use rubella vaccine. So immigrants from these areas are more likely to be susceptible to rubella than U.S. natives. The good news is that as of 2002, 42 of the 44 reporting countries in the Western Hemisphere have introduced rubella containing vaccine into their national programs. But many foreign born adults remain susceptible to rubella. Vaccination programs targeting immigrants from these areas – particularly programs in workplaces – could help reduce susceptibility and prevent rubella and CRS in these persons.

The first rubella vaccines were licensed in the U.S. in 1969. RA 27/3, known as Meruvax II, was licensed in 1979, and replaced the other vaccines. RA 27/3 vaccine is now the only rubella vaccine available in the U.S. It is different

because it is attenuated in a human diploid cell line, not in animal tissue culture. Rubella is a live virus vaccine, usually given in combination with measles and mumps vaccines as MMR. Single dose efficacy is estimated to be 95%, with a range of 90% to 97%. That means almost everyone who gets a dose will be protected. The duration of immunity, as with other live virus vaccines, is believed to be lifelong. The schedule is 1 dose on or after the first birthday. But remember that the second dose of measles vaccine is recommended to be given as MMR. So most people will receive a second dose of rubella as well.

The indications for rubella vaccine are all children 12 months of age or older without contraindications, and older children and adults without evidence of rubella immunity. Here is the definition of rubella immunity. A person can be considered immune to rubella if they have serologic evidence of immunity, documentation of one dose of rubella containing vaccine, or were born before 1957. Unlike measles and mumps, physician or personal history of rubella disease is not considered reliable and should not be accepted as evidence of rubella immunity. The acceptance of birth before 1957 as presumed evidence of immunity is a relatively recent change. In the past, ACIP has recommended that there be no cutoff year for rubella. But serologic studies indicate that more than 90% of persons born before 1970 are immune to rubella. But birth before 1957 does not guarantee rubella immunity, just like it does not guarantee immunity to measles or mumps. Because of the potential for congenital rubella syndrome if a woman is infected during pregnancy, ACIP recommends that birth before 1957 **not** be accepted as evidence of rubella immunity for women who might become pregnant. For women of childbearing age, ACIP recommends that only serology or documentation of at least one dose of rubella vaccine should be accepted as evidence of immunity. Using a strict definition of rubella immunity adds another layer of safety to our congenital rubella syndrome prevention efforts. CRS is a disease we would prefer to never see again.

A couple of comments on serologic testing. Occasionally you will encounter a person with a documented history of vaccination who has a negative rubella screening serology. Just go ahead and give them another dose of MMR, although the problem is most likely an insensitive test rather than true susceptibility. Once a person has been tested and found to be immune, no further testing needs to be done. There is no evidence that immunity to rubella wanes with time since vaccination.

You will recall from our General Recommendations session that adverse reactions following live attenuated vaccines are a mild form of disease. Here is a summary of adverse reactions following rubella vaccine. The highlighted symptoms have been associated with the rubella component. Fever occurs in 5% to 15% of recipients, and rash is reported in 5%. Both of these reactions are usually caused by the measles component, but may be caused by mumps or rubella vaccine virus. Joint symptoms occur in up to 25% of rubella susceptible women, less in men, and rarely in children. The most common joint symptoms reported after rubella or MMR vaccination are arthralgia, or joint pain, and arthritis, or joint swelling and redness. Remember that joint symptoms are more

common after natural disease, occurring in up to 70% of adult women. The onset of joint symptoms takes 1 to 3 weeks after vaccination, or an incubation period. Symptoms last from 1 day to about 3 weeks and rarely recur. These symptoms are usually not severe enough to cause absence from work. There have been reports from some investigators of persistent pain or chronic arthritis in women who received rubella vaccine. However, several large epidemiologic studies have not found an association between chronic joint symptoms and rubella vaccination. The preponderance of evidence indicates that rubella vaccine is not a cause of chronic arthritis.

The contraindications for rubella vaccine are identical to those for measles vaccine. A severe allergic reaction to a vaccine component or following a prior dose is a contraindication. Pregnancy and immunosuppression are also contraindications to rubella-containing vaccines. Moderate or severe acute illness and recent blood product are precautions. The pregnancy contraindication can be problematic for providers who see women of childbearing age. Let's review the recommended procedure for screening and vaccination of such women. ACIP recommends that you ask if the woman is pregnant or likely to become pregnant in the next 4 weeks. It may be a good idea to ask what form of contraception is being used. This is because women who are sexually active and not using contraception still might tell you they could not become pregnant in the next month. Exclude women who are or may become pregnant in the next 4 weeks. For those women who are not excluded by these questions, explain the theoretical risks of vaccination during pregnancy, and the importance of not becoming pregnant during the 4 weeks following vaccination. Then vaccinate them. ACIP does **not** recommend routine pregnancy testing of women before rubella vaccination.

Inadvertent vaccination of women who are pregnant is bound to occur, even with careful screening. Several studies have examined the risk of CRS following vaccination, including an American study, conducted from 1971 through 1989. It was called the Vaccine in Pregnancy, or VIP study. 321 women were enrolled after they were inadvertently vaccinated near or after conception. There were 324 live births including 3 sets of twins. There were no cases of CRS observed among these births. If you calculate the 95% confidence limits, you find that the risk of CRS in this situation is between 0% to 1.2%. That is what we are referring to when we say there is a theoretical risk. In reality, no case of CRS following rubella vaccination in pregnancy has ever been documented.

None of us intend to vaccinate a pregnant woman. But what if – despite your diligent screening – you do? You should reassure her that no case of congenital rubella syndrome has ever been reported in a woman vaccinated during pregnancy. You should also let her know – in terms she will understand – that the ACIP does not consider rubella vaccination alone sufficient reason to terminate a pregnancy. Of course, the final decision about management of the pregnancy lies with the woman and her physician.

Q: Many adult women are receiving a second dose of MMR vaccine for employment or college entrance. Is there any concern about joint symptoms following these second doses?

A: There is very little risk. Almost everyone becomes immune to rubella after their first dose. And immune women do not have joint symptoms after vaccination. So the chance of joint symptoms after a second dose are quite small. The only women who would be at risk for joint symptoms are the small number who failed to respond to the first dose.